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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,314	04/01/2002	Charles Tokumbo Adesuyl	CFV-013.01 (19935-1301	6933

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EXAMINER	
BERKO, RETFORD O	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 08/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,314	ADESUYL ET AL.	
	Examiner	Art Unit	
	Retford Berko	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *5/7/02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Acknowledgement: The Information Disclosure Statement filed March 7, 2002 is acknowledged and initialed.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6 and12-16 are rejected under 35 U.S.C. 102(b) as being anticipated Barry et al (US 5, 055, 306).

The claims are directed toward a controlled release pellet comprising a core (contains a poorly soluble drug and polyethylene glycol) and a coating (surrounds the core and coating comprises a water soluble cellulose and a water insoluble acrylic polymer). The claims are also directed toward the controlled release pellet containing a carrier i.e. water-insoluble, swellable cellulose (10-60% by wt of the core). The drug delivered to be delivered can be nifedipine, ibuprofen or oxaprozin (solubility less than 1.0 mg/ml at room temperature and pH 7.0). The claims are further drawn toward the delivery pellet having the ratio of water-insoluble acrylic polymer to water-soluble cellulose in the coating as in the range from 1:1 to 10:1; the coating on the pellet is 3-40% by weight of the pellet.

As in claim 1, Barry et al (Patent '306) teach controlled release formulation comprising a core comprising poorly soluble drug (ibuprofen) and a coating comprising hydroxylated cellulose i.e. hydroxymethylcelulose and water-insoluble acrylic polymer, i.e. Eudragit NE 30D

(abstract, col 6, lin 50-65 continuing to col 7, lin 1-5); the coating is a mixture of the water-soluble cellulose and water insoluble acrylic polymer (thus the ratio is 50:50; col 3, lin 50 and col 9, lin 35-40). According to Barry, the invention is in a pellet or granule form (col 8, lin 50-68) and may contain, in addition to the drug, polyethylene glycol; Avicel and Ac-Di-Sol (col 6, lin 10-30); ---these are the ingredients of applicant's Working Example No. 4 recited in the specification (page 12).

As in claim 6, Patent '306 teaches a carrier similar to that used by applicant; i.e. Avicel and Ac-Di-Sol (col 6, lin 20-30).

As in claim 12, Patent '306 teaches that the granule or pellet comprises of ibuprofen or nefedipine as drugs present at 10-50 wt/% of the pellet (col 9, lin15-20 and col11, lin 30-35). These examples of drug are the same drugs provided in applicant's specification at page 10 and page12; thus implicitly, the solubility and pH limitations in claims 12-14 are taught in Patent '306.

Patent '306 teaches the claim limitations in claims 15-16 in that for preparing the coating, the hydroxymethylcellulose was dissolved in water and then mixed with the Eudragit (col 9, lin 40) and the weight of the coating is 2-25% of the weight of the core of the pellet (col 3, lin 65-68).

Claims 1, 6 and 12-16 are anticipated by Patent 306.

Claim Rejections - 35 USC § 103

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

3. Claims 1-16 are rejected under 35 U.S.C.103(a) as being unpatentable over Barry et al (US 5, 055, 306) in view of Rudnic et al (US 5, 912, 013) further in view of Patel et al (6, 248, 363; filed November 23, 1999).

The claims are directed toward a controlled release pellet comprising a core (contains a poorly soluble drug and polyethylene glycol) and a coating (surrounds the core and coating comprises a water soluble cellulose and a water insoluble acrylic polymer). The claims are also directed toward the controlled release pellet containing a carrier i.e. water-insoluble, swellable

cellulose (10-60% by wt of the core). The drug delivered to be delivered can be nifedipine, ibuprofen or oxaprozin (solubility less than 1.0 mg/ml at room temperature and pH 7.0). The claims are further drawn toward the delivery pellet having the ratio of water-insoluble acrylic polymer to water-soluble cellulose in the coating as in the range from 1:1 to 10:1; the coating on the pellet is 3-40% by weight of the pellet. The claims are further directed toward the pellet having the core further comprising a disintegrant; e.g. croscarmellose sodium; sodium starch glycolate or crospovidone and wherein the disintegrant is 1-5% by weight of the core and wherein the polyethylene glycol used has molecular weight 1000-8000.

The disclosures of Barry et al (Patent '306) were discussed above. Patent '306 does not teach the use of disintegrant and does not teach the use of a specific polyethylene glycol

Rudnick et al (Patent '013) disclose controlled release drug delivery system in pellet formulation, for delivery of hydrophobic drug carbamazepine to patients and maintaining blood concentration of 12 micro grams/ml in patients for 12 hrs. Carbamazepine is a drug generally known in the art as having poor water solubility. Patent '013 discloses that the pellet has a core (col 8, lin 15-20) and is coated with a hydroxymethylcellulose and methacrylic acid polymer (Eudragit) and that the coating material can be employed at the range about 1.0-25% (col 3, lin 27-45) and col 7, lin 40-55). According to Rudnic et al, an embodiment of the drug delivery system as pellet core comprises of microcrystalline cellulose, hydroxypropylcellulose and drug (col 10, example 11 and is coated with hydroxypropylmethylcellulose, ethylcellulose and polyethylene-glycol-400 (col 10, example13).

Patent '013 also provides other working examples of the pellet core comprising of ingredients as claimed by applicant (col 13, example 31) except that Patent '013 does not

disclose the use of: (a) polyethylene glycol having molecular weight 1000-8000 (b) disintegrants and (c) specific working examples of ibuprofen or oxaprozin.

Patel et al (Patent '363) disclose solid carriers for improved delivery of pharmaceutical active ingredients having poor aqueous solubility (abstract and col 4, lin 57-65). Patent '363 discloses formulations such as coated pellet (col 36, lin 25-30, col 41, lin 45-69; col 42, lin 35-45 and col 43; lin 1-15). Significantly, Patent '363 discloses the use of solubilizers (col 38, lin 1-5), disintegrants (col 40, lin 30-35) and provides specific working examples of oxaprozin wherein the composition comprises of the drug and polyethylene glycol-40).

One of ordinary skill in the art would have been motivated to prepare controlled release drug delivery systems for delivery of drugs having poor solubility as disclosed in the prior art cited. By using the combination of methods disclosed in the prior art cited, one of ordinary skill would expect to obtain reasonable success in achieving improved drug delivery of otherwise insoluble drugs for sustained release treatment in patients by maintaining therapeutically effective concentrations in blood in order to meet patient needs. Thus, the need to use carriers that insure improved delivery of drugs for effective treatment of patients provides the motivation to combine the methods cited as prior. Because one of ordinary skill in the art possesses the ability to manipulate the amounts of the ingredients and coating of the compositions to achieve improved delivery of drugs as disclosed by the prior art, the invention as a whole would have been prima facie obvious to one of ordinary skill at the time it was invented.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Retford Berko** whose telephone number is 703-305-4442. The examiner can normally be reached on M-F from 8.00 am to 5.30 pm

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Thurman K Page**, can be reached on 571-272-0602. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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